REMARKS

This response addresses the issues raised by the Examiner in the Office Action electronically delivered November 7, 2007. Claim 119 is currently amended. Claims 126 to 128 have been cancelled. New claims 129 to 138 have been added.

Support for new claim 129 can be found at page 5, lines 14-17 of the specification. Support for new claims 130 to 132 can be found at page 6, lines 25-27 and page 13 lines 19-21 of the specification. Support for new claims 133 to 135 can be found at page 6, lines 11-16 of the specification. Support for new claims 136 to 138 can be found at page 5, lines 20-24.

Reply to 35 U.S.C. § 103 Rejection

The Examiner rejected currently pending claims 40-43, 45-69, 71-82 and 119-125, in light of Hudis et al. '99 combined with Henderson et al. and Winer et al., under 35 U.S.C. § 103(a). Applicant respectfully overcomes this rejection for the following reasons.

Hudis et al. '99 discloses a sequential and dose-dense treatment regimen for breast cancer consisting of 3 cycles of doxorubicin 90 mg/m^2, followed by 3 cycles of paclitaxel 250 mg/m^2, and finally 3 cycles of cyclophosphamide 3 g/m^2. (Page 93, abstract.) In justifying its use of 250 mg/m^2 paclitaxel, Hudis et al. '99 states that "for advanced disease, there seems to be an advantage for 175 mg/m^2 compared with the 135 mg/m^2 when it is administered over 3 hours, *and even higher doses may offer a small additional benefit.*" (Page 98, col. 1, first paragraph.) Hudis et al. '99 concludes that "on the basis of the earlier clinical trials of paclitaxel, we chose to use [high dose paclitaxel] in this pilot trial." (*Id.*)

One of the "earlier clinical trials" referred to in Hudis et al. '99 is Winer et al. Winer et al. discloses a non-dose-dense randomized trial of three doses of paclitaxel—175 mg/m^2, 210 mg/m^2 and 250 mg/m^2—in patients with metastatic breast cancer. Winer at al. further discloses that "[t]here is a significant correlation (P=.001) between

paclitaxel dose and time to disease progression," and that "[d]espite the greater degree of toxicity, formal quality of life analysis reveals no difference in patient-rated quality of life across the three arms." Winer et al. also notes that "[a]lthough there is a longer time to progression with higher doses, this potential advantage must be considered carefully in light of greater toxicity seen with increasing dose."

The Examiner argues that Hudis et al. '99 does not teach that lower doses of paclitaxel are inferior, but merely that the authors of the Hudis et al. '99 reference did not know whether or not they were equivalent to higher doses. (11/7/2007 Office Action at 7.) Applicant respectfully disagrees.

Hudis et al. '99 and Winer et al. clearly teach that higher doses of paclitaxel increase the time to disease progression. This is irrefutable. The Examiner, however, argues that, with respect to Winer et al., "[a]lthough the time to progression was longer, this benefit was offset by the greater toxicity at the higher doses." (11/7/2007 Office Action at 4.) This is not what Winer et al. expressly teaches, however. Winer et al. merely states that "[a]lthough there is a longer time to progression with higher doses, this potential advantage *must be considered carefully* in light of greater toxicity seen with increasing dose." Clearly, the authors of Hudis et al. '99 weighed the benefit of longer time to disease progression against the harm of increased toxicity and determined that the benefit of high dose paclitaxel outweighed the harm. The authors of Hudis et al. '99 did not believe that the increased time to disease progression "was offset by the greater toxicity at the higher doses," as the Examiner argues. This is understandable given Winer et al.'s disclosure that "[d]espite the greater degree of toxicity, formal quality of life analysis reveals no difference in patient-rated quality of life across the three arms."

According to the Federal Circuit, "A reference may be said to teach away when a person of ordinary skill, upon reading the reference . . . would be led in a direction divergent from the path that was taken by the applicant." *Tec Air, Inc. v. Denson Mfg. Michigan Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999). There can be no doubt that, with respect to paclitaxel, Hudis et al. '99 "le[ads] in a direction divergent from the path that was taken by the applicant," since it teaches that the increased time to disease progression

associated with higher doses of paclitaxel outweighs the increased toxicity. If this were not the case, the authors of Hudis et al. '99 would have used paclitaxel 175 mg/m^2, since Winer et. al—the reference they rely on in determining the appropriate dose of paclitaxel—explicitly found that "higher doses of paclitaxel do not improve response or survival in patients with metastatic breast cancer."

For the foregoing reasons, Applicant respectfully submits that currently pending claims 40-43, 45-69, 71-82 and 119-125 are unobvious in light of Hudis et al. '99, Henderson et al. and Winer et al. and requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

Conclusion

In view of the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below. If there are any fees due, please charge any such fees to our deposit account No. 501561 and reference attorney docket number 93580.010100.

Respectfully,

Date: February 7, 2008

By: _____

Hashim A. Rahman
Registration No. 60,405
Attorney for Applicant
Greenberg Traurig, LLP
200 Park Avenue
New York, New York 10166
Telephone No. 212-801-2146